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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/326,502	06/04/99	KROLL	COUL-005/04U

EXAMINER	
ZEMAN, M	

ART UNIT	PAPER NUMBER
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DATE MAILED: 09/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/326,502	Applicant(s) KROLL ET AL.	
	Examiner Mary K Zeman	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24,83 and 84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24,83 and 84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1631, Examiner Mary K Zeman. Claims 1-24 and 83-84 are pending in this application. Claims 83-84 are newly added. Claims 25-82 have been canceled.

The IDS filed 7/20/01 has been entered and considered. An initialed copy of the form PTO-1449 is included with this action.

Applicant's arguments filed 7/20/01 have been fully considered but they are not completely persuasive. Any non-reiterated rejections have been withdrawn.

The drawings have been approved by the Draftsman. Applicant is reminded that the Brief Description of the Drawings in the specification must refer specifically to each figure separately. At page 3, Figures 2-5 are discussed collectively, which is not proper.

Claim Rejections - 35 USC § 112

Claims 1-24, 83 and 84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the final clause states that the optimally effective dose is calculated by the therapeutic dose equation. However, the steps of the claim requires the calculation of the clearance profile which is not included (or not clearly included) in this final equation.

Further, it would appear that the initial step of the method of claim 1 should be to administer a tracer dose of the radiopharmaceutical, and collect data as to its clearance, because this information is **required** prior to being able to calculate the optimally effective dose.

As set forth previously, it is unclear from the claim language whether the "optimally effective dose" is equal to the "therapeutic dose". If they are equal, the equation in claim 1 should be amended to indicate that what is calculated is the same as that which is mentioned in the preamble of the claim. If they are not equal, Applicant must explain what the difference is between the two terms, and an additional limitation setting forth how to obtain the optimally effective dose from the therapeutic dose should be added to the independent claims.

The above comments regarding claim 1 equally apply to claim 19.

Both claims 2 and 7 add the limitation of doing a dose-escalation study, but for differing purposes. Would the same dose escalation study be done twice? Or can the results of the same study be used for both calculations? It is unclear how both the maximum effective mass of the patient and the clearance profile would be determined by such a dose-escalation study.

In claim 3 it is entirely unclear what property of the radiopharmaceutical is to be used for determining the maximum effective mass of the patient. The type of radioactive element? The type of biological to which it is attached? (e.g. an antibody and its activities?) The half-life of the radiopharmaceutical?

In claims 10, 13, 15 and 18, it would appear that some administration of a pharmaceutical is required, but no such limitation is present in those claims or claim 1 from which they depend. If no radiopharmaceutical is administered, there would be no radioactivity in the body to measure.

In claim 18, it is unclear how one is to "use" the mathematical functions described. It is suggested that something akin to "using the trapezoidal rule or Simpson's rule to calculate the residence time" be added to correlate the intent of the preamble with the limitations in the claim.

New claim 84 sets forth "the method of claim 19" in the preamble, which is incorrect. Claim 19 is drawn to a dose of a radiopharmaceutical, which is a product, not a process claim. Further, this claim does not appear to further limit the scope of claim 19, and is therefore improper.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-24, 83, 84, are rejected under 35 U.S.C. 102(b) as being anticipated by Wahl et al. (WO 96/34632 A1).

The claims are drawn to methods of calculating a optimally effective dose for the administration of a radiopharmaceutical. The calculations include determining a maximum tolerated dose, desired total body dose, clearance profile, patient mass, and effective mass, activity hours, residence time, leading to the calculation of the optimal effective dose.

Wahl et al. (WO 96/34632, PTO-1449) disclose methods of calculating the optimal effective dose of a radiopharmaceutical. The method can be computer-implemented. The calculations that are required by Wahl include: using a tracer dose to calculate a whole body dose, and desired body dose; an effective dose based on lean body mass; the clearance rate of the pharmaceutical (using up to eight timepoints); an injected activity and/or activity hour measurement; the residence time represented by the effective half life measurement; which are all correlated to determine the recommended dose of the radiopharmaceutical. A particular radiopharmaceutical is 131I-B1 antibody. All of these calculations appear to be performed in the same manner as those disclosed in the specification, and are therefore anticipatory of the above rejected claims in the absence of evidence to the contrary.

Claim 19 remains rejected under 35 U.S.C. 102(b) as being anticipated by Order (I.J. Radiation Oncology Bio. Phys, 6:703-710, 1980, PTO-1449 reference D11) for the reasons set forth in the previous office action.

Applicant's arguments are not persuasive. The claim is drawn to a product: an effective dose of a radiopharmaceutical. The recited method steps do not appear to materially affect the nature of the composition. The MPEP discusses product-by -process claims in chapter 2100: "Even though product-by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by -process claim is the same as, or obvious from a product in the prior art, the claim is unpatentable even though the prior product was made by a different process." See MPEP 2113.

Order teaches a therapeutically effective dose of a radiopharmaceutical in a patient and demonstrates the optimal therapy of intrahepatic malignancies with radiolabelled antibodies. No major organ toxicity was noted (see abstract). Thus, Order teaches an optimally effective

therapeutic dose of a radiopharmaceutical for administration to a patient and meets the limitations of the claim.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Toohey et al. 1999 Int. Radiopharm. Dosim. Symp. Proc. Conf. Meeting date 1996, Vol 2, pages 532-551. This document discloses methods of determining effective dosages for radiopharmaceuticals.

PK Solutions 2.0 software, Summit Research Services, released 4 June 1997, Online Users Guide. This document discloses a variety of calculations regarding pharmacokinetics used to calculate dosages for pharmaceuticals.

Clairand et al. J. Nuclear Med. 1999, Vol. 40, pages 1517-1523. This document discloses software and methods for calculating radiopharmaceutical dosages.

Liu et al. J. Nuclear Med. 1999, Vol 40, pages 1151-1153. This document discloses software and methods for calculating radiopharmaceutical dosages.

Document RSICC CODE PACKAGE CCC-528, retrieved from www-rsice.ornl.gov/codes/ccc/ccc5/ccc-528.html This document discloses characteristics of MIRDOSE 3.1 a program used to calculate dosages.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (703) 305-7133. The examiner can generally be reached between the hours of 7:30 am and 5:00 pm Monday through Thursday, and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at (703) 308-4028.

Official fax numbers for this Art Unit are: (703) 308-4242, (703) 872-9306. An *unofficial* fax number, direct to the Examiner is (703) 746 5279. Please call prior to use of this number.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the TC1600 Receptionist whose telephone number is (703) 308-0196.

mkz
9/5/01

MARY K. ZEMAN
PATENT EXAMINER
9/5/01